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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,935	10/02/2003	David Bar-Or	6134-81	7439

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EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
03/01/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/680,935	BAR-OR ET AL.	
	Examiner	**Art Unit**	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _19 January 2011_.
2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _164,177 and 307-328_ is/are pending in the application.
  4a) Of the above claim(s) _312-316 and 324-328_ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) _166,177,307-311 and 317-323_ is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
  Paper No(s)/Mail Date _10/6/10_.
4) ☐ Interview Summary (PTO-413)
  Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 1/19/11, are acknowledged.

Claims 164, 177, and 307-328 are pending.

2. Claims 312-316 and 324-328 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 166, 177, 307-311, and 317-323 are being acted upon.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 164, 177, 307-311, and 317-323 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Peters, 1995, in view of U.S. Patent 5,223,392 and U.S. Publication 2003/0124616 (of record).

As set forth previously, Peters teaches that human albumin exists as several modified forms in the blood, including a form comprising disulfide bound cysteine at an unpaired cysteine at position 34 (i.e. a cysteinylated albumin, see page 51, in particular). Peters further teaches that considerable investigative effort has been directed toward understanding the properties and molecular environment of this cysteine residue, and that various amperometric assays, colormetric assays, or ion exchange techniques can be used to determine the sulfhydryl content of albumin.

Peters et al. does not teach an antibody specific to the cysteinylated form of albumin.

The ‘392 patent teaches producing antibodies specific for a modified form of albumin, and that said antibodies are capable of distinguishing modified and unmodified albumin (see column 7 in particular). The ‘392 patent teaches using said antibodies to measure modified forms of albumin in the circulation, and that the measurement is accurate and specific and avoids the drawbacks of reproducibility, cost, expensive, instrumentation, and accuracy as associated with other types of assays (see column 2, in particular). The ‘392 patent teaches that monoclonal antibodies or antibody fragments are suitable for measuring modified albumin (see column 5, in particular).

The ‘616 patent teaches detecting homocysteinylated proteins, including homocysteinylated albumin, with an antibody that specifically binds to said homocysteinylated proteins (see paragraphs 6, 8, 13, and 45-46, in particular). The ‘616 publication also teaches kits comprising said antibodies (see paragraph 13, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make an antibody, antibody fragment, or kit comprising said antibody, as taught by the ‘392 patent and the ‘616 patent, specific to cysteinylated albumin, as taught by Peters The ordinary artisan at the time the invention was made would have been motivated to make an antibody to cysteinylated albumin in order to have an accurate and specific means of measuring cysteinylated albumin in the blood and to avoid the problems of reproducibility, cost, expense, instrumentation, and accuracy involved with other methods of measuring modified forms of albumin. Furthermore, the ordinary artisan would have had a reasonable expectation of success in producing said antibodies given that the '616 patent teaches a method to produce antibodies which specifically recognize a homocysteylated form of albumin, and homocysteine is a structurally similar analog to cysteine. Furthermore, regarding the limitations of instructions specifying an intended use of the claimed kit (i.e. for diagnosing ischemia or multiple organ failure), where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art see MPEP 2112.01).

Applicant’s arguments filed 1/19/11 have been fully considered, but they are not persuasive.

Applicant argues that Peters does not teach an antibody that can distinguish between the cysteinylated and non-cysteinylated forms of albumin, but merely that such forms of albumin exist. Applicant notes that the ‘392 patent teach production of antibodies for modified forms of albumin, such as glycated albumin, but does not teach antibodies that recognize cysteinylated forms of albumin. Applicant notes that the ‘616 publication teaches antibodies to homocysteinylated albumin, which is different than cysteinylated albumin.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Peters teaches a modified form of albumin, cysteinylated albumin, and the desirability of measuring the amount of cysteinylated albumin. The ‘616 patent and the ‘392 patent teach antibodies to various modified forms of albumin, and teach that antibodies are advantageous for measuring modified forms of albumin since they avoid the drawbacks of reproducibility, cost, expensive, instrumentation, and accuracy as associated with other types of assays. Thus, the ordinary artisan would have been motivated to produce an antibody to the modified form of albumin of Peters, as taught by the ‘392 patent and the ‘616 patent.

Applicant further argues that nonce of the references provide guidance on how to make antibodies that bind to cysteinylated albumin and one of skill in the art would not find it obvious to do so, nor would they have any expectation of successfully doing so.

The ‘392 patent provides ample guidance for one of ordinary skill in the art to make an antibody specific for a modified form of albumin. The ‘392 patent teaches that methods of making monoclonal antibodies are well known to those of ordinary skill in the art, and that antibodies specific to a modified form of albumin (glycated albumin) can be produced by immunizing mice with the modified albumin and screening the produced antibodies for those that bind the modified form of albumin but not the un-modified form (see columns 4-5, in particular). The ‘616 publication teaches the feasibility and desirability of producing antibodies that specifically bind to the homocysteinylated forms of proteins, including albumin (see pages 2-3, in particular). The '616 publication likewise provides guidance for producing such antibodies, teaching that they can be produced by immunizing animals with the homocysteinylated protein using techniques known or widely available in the art (see page 3, in particular). Furthermore, homocysteine is a structurally similar analog to cysteine, and the ordinary artisan would expect that the same technique of monoclonal antibody production suitable for generating antibodies specific for homocysteinylated proteins could be applied to generate an antibody specific for a cysteinylated protein. Thus, the ordinary artisan would have a reasonable expectation of success in applying the teachings of the '392 patent and the '616 publication regarding antibody production, to make an antibody to the cysteinylated albumin taught by Peters (i.e. by immunizing an animal with cysteinylated albumin and screening the resulting antibodies for those that specifically recognized cysteinylated albumin, but not non-cysteinylated albumin, as taught by the '392 patent and the '616 publication). Furthermore, the ordinary artisan would be motivated to do so, since Peters teach the desirability of measuring the amount of cysteinylated albumin, and the '392 patent teaches that using antibodies to measure modified forms of albumin is accurate and specific and avoids the drawbacks of reproducibility, cost, expensive, instrumentation, and accuracy as associated with other types of assays (see column 2, in particular).

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-

4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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